ABSTRACT

THESIS: Characterization of Ume6 and Ume7 in *Candida albicans* morphology and the development of *C. albicans* CRISPR/SpRY

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Candida albicans is the most frequently isolated human fungal pathogen. The ability of *C. albicans* to reversibly switch between a variety of morphologies is a major virulence factor and enables colonization of a wide range of host environments. Filamentation is the ability of *C. albicans* to reversibly switch from a budding yeast cell to an elongated filament. Filaments can invade and damage host tissues and are required to maintain long-term infection. White/opaque switching is the reversible switch from a standard white yeast cell to an oblong opaque cell. The white to opaque switch is required for mating. Additionally, white and opaque cells differ in metabolic requirements and may be important for colonization in diverse host environments. *C. albicans* polymorphism is controlled by complex networks of transcriptional regulators. *C. albicans* Ume6 is an important transcriptional regulator of filamentation. Ume6 contains a zinc finger domain which has not been extensively characterized. In this thesis I characterized the roles of the Ume6 zinc finger and C-terminus domains in filamentation. I found the Ume6 C-terminus is required for efficient filamentation. I

wanted to introduce more mutations into the *UME6* 3' region. However, the *UME6* 3' region is AT-rich and targeting it with CRISPR/Cas9 has been challenging, as Cas9 requires the presence of an NGG protospacer adjacent motif, PAM. To overcome this, I developed a CRISPR/SpRY system for *C. albicans* and show that this system enables efficient mutation at nonNGG PAM sequences. Finally, I aimed to determine if Ume7, an uncharacterized homolog of Ume6, is involved in maintenance of *C. albicans* morphology. I found *ume7* mutants were not defective for filamentation or white/opaque switching, indicating that Ume7 has a function distinct from Ume6.